UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,360	06/27/2001	Michel Lazdunski	1256-R-00	2195

35811 7590 07/19/2004

IP DEPARTMENT OF PIPER RUDNICK LLP
ONE LIBERTY PLACE, SUITE 4900
1650 MARKET ST
PHILADELPHIA, PA 19103

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,360	LAZDUNSKI ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *4-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 27* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-3 and 27, drawn to an isolated and purified protein comprising a mammalian K+ channel in the reply filed on 04 June 2004 is acknowledged.

Claims 4-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 04 June 2004.

Claims 1-3 and 27 are under consideration in the instant application.

Sequence Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). **Specifically, the sequences disclosed in Figure 1A are not accompanied by the required reference to the relevant sequence identifiers.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Claim Objections

2. Claim 3 is objected to because of the following informalities:

3. In claim 3, the sequence identifier should be amended to recite, for example, "SEQ ID NO: ".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-2 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified protein comprising a mammalian K+ channel with two pore domains, wherein said channel (a) produces currents whose current-voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions and (b) comprises the amino acid sequence of SEQ ID NO: 2, *does not* reasonably provide enablement for an isolated and purified protein comprising a mammalian K+ channel with two pore domains, wherein said channel produces currents whose current voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to an isolated and purified protein comprising a mammalian K+ channel with two pore domains, wherein said channel produces currents whose current voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions. The claims recite that the channel is a human K+ channel. The claims also recite that high symmetrical K+ conditions is a K+-rich external medium of around 150mM.

The specification of the instant application teaches that the nucleic acid sequence deduced from the cDNA fragments of human brain is 2730 bp long and contains an open reading frame of 1617 nucleotides, predicting a 538 amino acid polypeptide (as shown in Fig. 1A) (pg

17, lines 1-2). The specification discloses that the polypeptide displays four membrane spanning segments (M1 to M4), two P domains (P1 and P2) and an extended loop between M1 and P1 (pg 17, lines 3-5). The specification also teaches that the polypeptide is a human K+ channel with two pore domains that produces currents whose current-voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions and comprises the sequence of amino acids in SEQ ID NO: 2 (pg 3, [0008]). However, the specification of the instant application does not disclose any methods or working examples to indicate the identification and purification of all possible mammalian K+ channels with two pore domains wherein the current-voltage relationship is weakly inwardly rectifying. Undue experimentation would be required of the skilled artisan to identify and purify all possible K+ channels with two pore domains and screen them for activity, particularly weak inward rectification properties. Relevant literature reports examples of polypeptide families wherein individual members have distinct amino acid sequences and/or diverse biological activities. For example, Lesage et al. (Am J Physiol Renal Physiol 279: 793-801, 2000) teach that TASK-1 and TASK-2 (both two-pore-domain K+ channels) have similar functional properties but are not particularly sequence related (pg 794, bottom of col 2). Lesage et al. disclose that sequence comparison is not sufficient for predicting the functional properties of two-pore-domain K+ channels (bottom of pg 794 through the top of pg 795). Additionally, Lesage et al. indicate that "because of their functional diversity and their widespread distribution, two-pore-domain K+ channels are expected to fulfill many physiological roles in addition to setting resting membrane potential. The elucidation of these roles will require finding a specific pharmacology for these channels to better analyze their roles in vivo" (pg 799, col 2, 1st paragraph).

Due to the large quantity of experimentation necessary to generate the infinite number of proteins recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, and the breadth of the claims embrace a broad class of proteins, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

5. Claims 1-2 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to an isolated and purified protein comprising a mammalian K+ channel with two pore domains, wherein said channel produces currents whose current voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions. The claims recite that the channel is a human K+ channel. The claims also recite that high symmetrical K+ conditions is a K+-rich external medium of around 150mM.

The specification teaches human a TREK-2 polynucleotide and polypeptide (SEQ ID NO: 1 and SEQ ID NO: 2, respectively). However, the specification does not teach functional or structural characteristics of all mammalian two-pore-domain K+ channel polynucleotides and polypeptides in the context of a cell or organism. The description of one TREK2 polynucleotide

species (SEQ ID NO: 1) and one TREK2 polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all mammalian two-pore-domain K+ channels producing currents whose current-voltage relationship is weakly inwardly rectifying.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated and purified mammalian K+ channel with two pore domains, wherein said channel (a) produces currents whose current-voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions and (b) comprises the amino acid sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Lesage et al. (EMBO J 15(5): 1004-1011, 1996).

Lesage et al. teach a human weakly inward rectifying K+ channel termed "TWIK-1" (pg 1004; Figure 1). Lesage et al. disclose that the protein includes two P (pore) domains (abstract; pg 1005, col 1; Figure 1). Lesage et al. also teach that the channel produces currents whose current-voltage relationship is weakly inwardly rectifying in high symmetrical K+ conditions (pg 1010; first full 2nd -3rd full paragraphs).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Fink et al. EMBO J. 17(12):3297-3308, 1998. (cloning of TRAAK)

Fink et al. EMBO J. 15(24): 6854-6862, 1996. (cloning of TREK-1)

Gu et al. J Physiol. 539(Pt 3):657-668, 2002. (splice variants of TREK-2)

Lesage et al. J Biol Chem. 275(37):28398-28405, 2000. (TREK-2)

Maylie et al. Nat Neurosci. 4(5):457-458, 2001.("reversible" TREK-1)

Patel et al. EMBO J. 17(15): 4283-4290, 1998. (TREK-1 opens by AA and other polyunsaturated acids)

Patel et al. Nat Neurosci. 2(5):422-426, 1999. (anesthetics activate TASK, TREK-1)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
15 July 2004

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600